



NDA 20-757/S-014

Bristol-Myers Squibb
Attention: Ms. Grace Heckman
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Ms. Heckman:

Please refer to your supplemental new drug application dated February 16, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) Tablets.

We acknowledge receipt of your submission dated April 25, 2001 that constituted a complete response to our December 15, 2000 approvable letter.

This supplemental new drug application provides for final printed labeling revised as follows:

1. Under **CLINICAL PHARMACOLOGY**, the **Special Populations**, the *Pediatric* subsection has been changed to:

The pharmacokinetics of irbesartan were studied in hypertensive children (age 6-12, n=9) and adolescents (age 13-16, n=12) following single and multiple daily doses of 2 mg/kg (maximum dose of 150 mg per day) for 4 weeks. Accumulation with repeated doses was limited (18%) in both age groups. Clearance rates, AUC values, and Cmax values were comparable to adults receiving 150 mg daily. Irbesartan pharmacokinetics have not been investigated in patients <6 years of age.

2. Under **PRECAUTIONS, Pediatric Use**, a second paragraph has been added that reads:

Pharmacokinetic parameters in pediatric subjects (age 6-16, n=21) were comparable to adults. At doses up to 150 mg daily for 4 weeks, AVAPRO (irbesartan) was well tolerated in hypertensive children and adolescents (see **CLINICAL PHARMACOLOGY; Special Populations**). Blood pressure reductions were comparable to adults receiving 150 mg daily; however, greater sensitivity in some patients cannot be ruled out (See **DOSAGE and ADMINISTRATION: Pediatric Patients**). AVAPRO has not been studied in pediatric patients less than 6 years old.

3. Under **DOSAGE and ADMINISTRATION**, a **Pediatric Patients** subsection has been added:

Children (< 6 years): safety and effectiveness have not been established.

Children (6-12 years): An initial dose of 75 mg once daily is reasonable. Patients requiring further reduction in blood pressure should be titrated to 150 mg once daily (see **PRECAUTIONS; Pediatric Use**).

Adolescent patients (13-16 years): An initial dose of 150 mg once daily is reasonable. Patients requiring further reduction in blood pressure should be titrated to 300 mg once daily. Higher doses are not recommended (see **PRECAUTIONS; Pediatric Use**).

4. Under **HOW SUPPLIED**, the 75 mg Blister Pack of 100 (NDC# 0087-2771-35) has been removed.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert included in your submission of April 25, 2001). Accordingly, the supplemental application is approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

{See appended electronic signature page}

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